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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,780	11/30/2001	Roman Sakowicz	CYTOP083	9903

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,780	SAKOWICZ ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/22/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) *12-15,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Upon further review of the application, the examiner vacated all the previous office actions and issuing a new non-final office action (see interview summary 3/29/05). The examiner regrets any inconvenience caused due to this.

Election

2. Applicant's election of Group II, claims 8-15 drawn to a protein, SEQ ID NO: 2 (9/19/03) with traverse is acknowledged.

The traversal is on the grounds that the restriction requirement of single disclosed SEQ.ID.NO: 2 is not proper as SEQ.ID.NO: 4, 6, 8 and 10 etc are fragments of SEQ.ID.NO: 2 and will not be an undue burden on the Office to search all the sequences. In accordance with MPEP 803.04 ten sequences should be examined.

This is not found persuasive because MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. The term "distinct" is defined to "mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of the Groups are drawn to distinct inventions, which are related as separate products capable of separate, use, or sale as described in the previous Office Action (8/19/03) Restriction between the inventions is deemed to be proper for the reasons previously set forth (8/19/03). Additionally, SEQ.ID.NO: 2, 4, 6, 8 and 10 etc are structurally distinct and different to each other and thus each is identified by a specific sequence identification number. Therefore, where structural identity is required such as expression, the

different sequences have different effects. Each sequence is unique, different and distinct having specific biological structure as evidence by the number of amino acids and therefore has added unique biological property and unique biological function of interacting with the enzymes and proteins etc that are involved in mitotic kinesin motility. In regard to burden of search, the sequence search and the literature search, particularly relevant in this motor proteins art, is not co-extensive, because, for example, search and examination issues for each peptide fragments are different and would not encompass the full length protein. Clearly different searches and issues are involved in the examination of each peptide fragment. MPEP 803.04 states that up to ten sequences will be examined. However, this is not the normal practice and is only for EST sequences. Further, up to 10 sequences may be searched under certain circumstances as seen fit by the Director and not for proteins that have unique biological property and unique biological function of interacting with various enzymes and proteins etc that are involved in mitotic kinesin motility.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

3. Applicant's response to restriction requirement filed on 9/19/03 is acknowledged.

Claims 8-15 and 17-18 are currently pending in the application.

Claims 11-15 have been amended.

Claims 1-7 and 16 have been cancelled.

Claims 8 -11 with respect to SEQ.ID.NO: 1 is under examination and will be prosecuted in this application.

Claims 12-15 and 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicant timely traversed the restriction (election) requirement in 9/19/03.

Claim Rejections - 35 USC 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying

5. Claims 8-11 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to isolated protein comprises a sequence SEQ.ID.NO: 2, that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2, said protein binds to polyclonal antibody against a protein comprising SEQ.ID.NO: 2.

The specification describes as part of the invention, an isolated recombinant kinesin motor protein consisting of SEQ ID NO: 2, which is encoded by SEQ.ID.NO: 1 (PfKin-I-1 construct) from *Plasmodium falciparurum* merozoite. The specification teaches that this full-length protein contains 1288 amino acids. Taxol stabilized motor protein microtubules (SEQ ID NO: 2 from PfKin-I-1 construct) have been shown to be depolymerized in a microtubule depolymerization assay. The specification speculates that this protein could be useful in diagnosis, prevention and treatment of malaria. However, the specification fails to disclose an isolated protein comprising a sequence t has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 having microtubule stimulated ATpase activity. Applicants broadly describe the invention as embracing any deletion by use of language in which a specified percent of amino acids can be changed in the protein. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116). Therefore, an isolated protein consisting of SEQ.ID.NO: 2 meets the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below:

The specification fails to teach an isolated protein comprising a sequence has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 microtubule stimulated ATpase activity and is noted that the claimed protein do not exist as an invention independent of their function (examiner considers this as a variant). The actual relevant identifying characteristics of claimed kinesin protein having the claimed properties (microtubule stimulated ATpase activity) of the protein can only be determined empirically by actually making recited variant and testing it to determine whether such a variant having the particularly disclosed properties of microtubule stimulated ATpase activity. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. This specification does not teach such, and the art is devoid of this correlation for an isolated protein comprising a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 with undetermined function. There is no written description support for an isolated protein comprising a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 as claimed. In addition, an isolated protein comprising (open language) a sequence SEQ.ID.NO: 2 plus unlimited and unknown amino acids would result in an unknown protein without sufficient structure and completely lacking identifying characteristics such as function, i.e. having microtubule stimulated ATPase activity. The specification fails to disclose any deletion or change in an amino acid sequence, SEQ.ID.NO: 2 to obtain said protein that could be

depolymerized in the presence of taxol to indicate its activity. The specification does not describe any use of said variant as claimed (comprising, open language) in identifying *Plasmodium* and do not meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach an isolated protein comprising a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 microtubule stimulated ATpase activity and does not satisfy the written description guidelines because the claimed protein variant has not been disclosed in this application. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

6. Claims 8-11 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling an isolated recombinant kinesin motor protein consisting of SEQ ID NO: 2, does not reasonably provide enablement for an isolated protein comprising a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly, connected, to make and use the invention commensurate in scope with these claims.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is preparing a recombinant kinesin motor protein, SEQ.ID.NO: 2 from merozoites of *Plasmodium falciparum.* The specification on pages 46 -48 teaches the claimed protein has microtubule depolymerizing activity. However, the specification does not disclose the claimed protein, SEQ.ID.NO: 2 having microtubule stimulated ATPase activity. The specification fails to provide an enabling disclosure other than an isolated recombinant kinesin motor protein consisting of SEQ ID NO: 2 because it fails to provide any guidance regarding how to make and use an isolated protein comprising (open language) a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 having microtubule stimulated ATPase activity (examiner is viewing them as variants and will be referred as variants).

The specification fails to provide guidance for an isolated protein comprising (open language) a sequence that has greater than 90%identity to SEQ ID NO: 2 plus unlimited and unknown amino acids would result in an unknown variants without any structure and other identifying characteristics such as function. Thus, variants as claimed are broader than SEQ.ID.NO: 2 and the specification fail to provide sufficient guidance such that one of ordinary skill in the art can predict a priori what protein variants can be made. Further, to make proteins

without structure and function are not routine in the art. Therefore, none of the criteria as suggested by the applicant are not satisfied.

The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any isolated protein comprising (open language) comprising a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 having microtubule stimulated ATPase activity. The specification fails to disclose that the claimed sequence having microtubule stimulated ATPase activity.

The state of the art indicates that kinesin, dynein and myosin each form large superfamilies and participate in many different intracellular transport system. Kinesins are a large super family of microtubule motor proteins that use the energy of ATP hydrolysis to produce force. They are defined by the presence of a catalytic core motor domain (historically known as the 'head' domain), which hydrolyzes ATP and binds to microtubules (MTs). Kinesins are classified into three subfamilies based on the position of their motor domain within the primary sequence of the protein. The Kin C subfamily comprises kinesins with a C-terminally located core motor domain; Kin N kinesins have an N-terminally located core motor domain; and Kin I kinesins possess an internally located core motor domain (Yulia Ovechkina and Linda Wordeman, *Traffic* 2003, Volume 4 Issue 6 Page 367)

The art also teaches motor protein location does not reliably predict function (Lin et al Cell Motil cytoskeleton 1996, 3494: 299-313). The specification does not disclose the claimed protein participate in which intracellular transport system. The specification also does not disclose plasmodium kinesin motor core domain in a large protein having 1288 amino acids. As taught by the prior art any substitution, insertion or deletion or change in a protein is highly complex and unpredictable and even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a

single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide. Furthermore, it is unclear whether protein varied by 90% similarity can be used to screen for identifying anti –microbial drugs or as diagnostic tools. Thus, protein varied by 90% similarity or identity at protein level must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for an isolated protein comprising (open language) a sequence that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2 having microtubule stimulated ATPase activity. The specification provides no disclosure how the claimed protein may be used as a target for a potential drug screening because it fails to provide guidance whether the claimed protein has ATPase activity etc. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Rodionov et al 1990, JB.C. 265 (10), 5702-5707.

The claims are drawn to isolated protein comprises a sequence SEQ.ID.NO: 2, that has greater than 90% amino acid sequence identity to SEQ.ID.NO: 2, said protein binds to polyclonal antibody against a protein comprising SEQ.ID.NO: 2.

Rodionov et al disclose an isolated kinesin protein in figure 3 c and figure 3e. This 116 kD protein cosediments with microtubles (see figure 3c and 3e) and has microtubule stimulated ATPase activity (see figure 4, page 5704, right column through page 5705, left column). The kinesin protein disclosed by the prior art read on the claimed invention protein because S.microtubles were able to glide along kinesin coated coverslip as shown in figure4. Thus, functionally, the disclosed prior art protein and the claimed protein are same. Characteristics such as protein comprising a sequence SEQ.ID.NO: 2 and binding to polyclonal antibody etc would be inherent in the protein preparation of Rodionov et al. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed protein and the protein of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 8-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Fowler et al Mol Biochem Parasitol. 2001 Oct; 117(2): 187-200.

Claims have been discussed supra.

Fowler et al disclose 135 kD kinesin protein of Plasmodium *falciparum* merozoite (see figure 1) and it reads on the claim kinesin protein because kinesin antibody bound to kinesin as shown in figure 1. Figure 2 discloses the presence of kinesin protein in all four stages of the asexual life cycle of the *Plasmodium.* The 135kD protein disclosed by prior art read on the claimed protein as it binds to antibody to kinesin and the molecular weight disclosed protein 135

kD is same as the claimed polypeptide, SEQ.ID.NO: 2 having 1288 amino acids because the molecular weight of each amino acid is approximately 110 daltons. Characteristics such as protein comprising the amino acid sequence SEQ.ID.NO: 2 would be inherent in the preparations of Fowler et al kinesin protein. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product, kit comprising antibodies and label and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Relevant Prior Art

10. The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

Moores etal, 2003 The Journal of Cell Biology, Volume 163, Number 5, 963-971 teach an elegant mechanistic basis for their unique depolymerizing activity. Kinl kinesins are important in regulating the complex dynamics of the microtubule cytoskeleton. They are unusual in that they depolymerize, rather than move along microtubules. To determine the attributes of Kinls that distinguish them from translocating kinesins, the ATPase activity, microtubule affinity, and three-dimensional microtubule-bound structure of a minimal Kinl motor domain has been examined. Together, the kinetic, affinity, and structural data lead to the conclusion that on binding to the microtubule lattice, Kinls release ADP and enter a stable, low-affinity, regulated state, from which they do not readily progress through the ATPase cycle. This state may favor detachment, or diffusion of the Kinl to its site of action, the microtubule ends. Unlike conventional translocating kinesins, which are microtubule lattice–stimulated ATPases, it seems that with Kinls, nucleotide-mediated modulation of tubulin affinity is only possible when it is coupled to protofilament deformation.

Pinder JC, et al J Cell Sci. 1998 Jul; 111 (Pt 13): 1831-9 teach the genome of the malaria parasite, Plasmodium falciparum, contains a myosin gene sequence, which bears a close homology to one of the myosin genes found in another apicomplexan parasite, Toxoplasma gondii. A polyclonal antibody was generated against an expressed polypeptide of molecular mass 27,000, based on part of the deduced sequence of this myosin. The antibody reacted with the cognate antigen and with a component of the total parasite protein on immunoblots, but not with vertebrate striated or smooth muscle myosins. It did, however, recognize two components in the cellular protein of Toxoplasma gondii. The antibody was used to investigate stage-specificity of expression of the myosin (here designated Pf-myo1) in P. falciparum. The results showed that the protein is synthesized in mature schizonts and is present in merozoites, but

vanishes after the parasite enters the red cell. Pf-myo1 was found to be largely, though not entirely, associated with the particulate parasite cell fraction and is thus presumably mainly membrane bound. It was not solubilised by media that would be expected to dissociate actomyosin or myosin filaments, or by non-ionic detergent. Immunofluorescence revealed that in the merozoite and mature schizont Pf-myo1 is predominantly located around the periphery of the cell. Immuno-gold electron microscopy also showed the presence of the myosin around almost the entire parasite periphery, and especially in the region surrounding the apical prominence. Labelling was concentrated under the plasma membrane but was not seen in the apical prominence itself. This suggests that Pf-myo1 is associated with the plasma membrane or with the outer membrane of the subplasmalemmal cisterna, which forms a lining to the plasma membrane, with a gap at the apical prominence. The results lead to a conjectural model of the invasion mechanism.

Rice et al *Nature*, 402, 778 - 784 (16 December 1999 teach Kinesin motors power many motile processes by converting ATP energy into unidirectional motion along microtubules. The force-generating and enzymatic properties of conventional kinesin have been extensively studied; however, the structural basis of movement is unknown. A visualized conformational change of a ~15-amino-acid region (the neck linker) in kinesin is observed using electron paramagnetic resonance, fluorescence resonance energy transfer, pre-steady state kinetics and cryo-electron microscopy. This region becomes immobilized and extended towards the microtubule 'plus' end when kinesin binds microtubules and ATP, and reverts to a more mobile conformation when γ-phosphate is released after nucleotide hydrolysis. This conformational change explains both the direction of kinesin motion and processive movement by the kinesin dimer.

Remarks

11. No Claims are allowed.

Conclusion

12. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D